REMARKS

Claims 6-14, 17-24, 29-30, 33-38, and 43-47 are cancelled without prejudice or disclaimer. The claims are amended in response to the Examiner's comments under § 112.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. Formal Matters

A. Election requirement In response to a election requirement, Applicants elected to prosecute the invention of example 50 on page 55 of the specification. Affirmation of that election is herein made.

B. Improper Markush group. Claims 1-37 and 39-47 were rejected as drawn to an improper Markush group. The compounds listed in the Markush group were not considered by the Examiner to be functionally equivalent. The improper Markush groups were cited as ring systems A^1, A^2, k, n, Q, Ar, Y, R^5, R^6, and R^8.

Claim 1 has been amended to remove non-elected subject matter. Accordingly, it is believed that the claims now recite proper Markush groupings, and that this rejection may be withdawn.

C. Allowable subject matter.

Claim 38 was objected to as dependent on a rejected claim. In response, claim 38 is amended as an independent claim.

II. Rejections Under 35 USC § 101.

Claims 43 and 45 were rejected for lack of a credible utiliyt or a well established utility. This rejection is rendered moot by cancellation of claims 43 and 45.

III. Rejection Under 35 USC § 112, first paragraph.

Claims 43 and 45 were rejected for lack of enablement. This rejection is rendered moot by cancellation of claims 43 and 45.

IV. Rejections Under 35 USC § 102(b).

A. Claims 1-5, 14, 17-34, 36, and 39-42 are rejected as anticipated by Wild et al. Claims 14, 17-24, 29-30, 33-34, and 36 are cancelled. Therefore, claims 1-5, 25-28, 31-32, and 39-42 remain rejected, which rejection is respectfully traversed on the grounds that Wild et al. does not describe a compound encompassed by the amended claims above. Accordingly, it is believed that in light of the above amendments, this rejection should be withdrawn.

Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: 20 March 2001

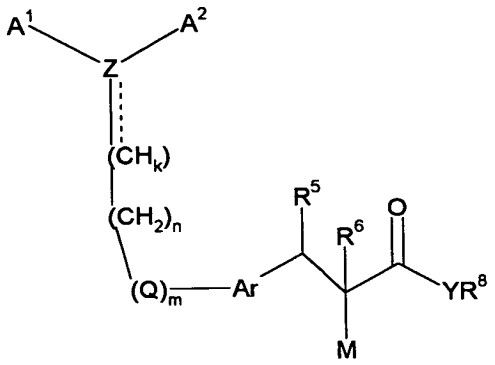
Valeta A. Gregg

Valeta A. Gregg, Reg. No. 35,127
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123

23650
PATENT TRADEMARK OFFICE

Version with Markings to Show Changes Made

1. (Amended) A compound of formula (I)



wherein A^1 and A^2 are independently of each other a 5-6 membered cyclic ring [or a 9-10 membered bicyclic ring,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C_{1-12}-alkyl, (C_{3-6}-cycloalkyl)C_{1-6}-alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl, C_{1-12}-alkoxy, aryl, aryloxy, arylalkyl, arylalkoxy, heterocyclyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, acyl, acyloxy, hydroxyC_{1-12}-alkyl, amino, acylamino, C_{1-12}-alkyl-amino, C_{1-6}-dialkylamino, arylamino, arylalkylamino, aminoC_{1-12}-alkyl, C_{1-12}-alkoxycarbonyl, alkylaminocarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, C_{1-12}-alkoxyC_{1-12}-alkyl, aryloxyC_{1-12}-alkyl, arylalkoxyC_{1-12}-alkyl, arylthio, C_{1-12}-alkylthio, thioC_{1-12}-alkyl, C_{1-12}-alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino, -COR^1, or -SO_2R^2, wherein R^1 and R^2 independently of each other are selected from hydroxy, halogen, perhalomethyl, C_{1-6}-alkoxy or amino optionally substituted with one or more C_{1-6}-alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

Z is C or CR^3, wherein R^3 is hydrogen, halogen, perhalomethyl, C_{1-12}-alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl, C_{1-12}-alkoxy, aryloxy, arylalkoxy, heteroaryloxy, heteroarylalkoxy, acyl, acyloxy, hydroxyC_{1-12}-alkyl, C_{1-12}-alkoxyC_{1-12}-alkyl, aryloxyC_{1-12}-alkyl, arylalkoxyC_{1-12}-alkyl, thioC_{1-12}-alkyl, -COR^4, or -SO_2R^{11}, wherein R^4 and R^{11} independently of each other are selected from hydroxy, halogen, perhalomethyl, C_{1-6}-alkoxy or amino optionally substituted with one or more C_{1-6}-alkyl, perhalomethyl or aryl optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

Q is O[,] or S [or NR^{12}, wherein R^{12} is hydrogen, perhalomethyl, C_{1-12}-alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl, aryl, arylalkyl, heterocyclyl, heteroaryl, heteroarylalkyl, acyl, hydroxyC_{1-12}-alkyl, aminoC_{1-12}-alkyl, C_{1-12}-alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, C_{1-12}-alkoxyC_{1-12}-alkyl, aryloxyC_{1-12}-alkyl, arylalkoxyC_{1-12}-alkyl, thioC_{1-12}-alkyl, $-COR^{13}$, or $-SO_2R^{14}$, wherein R^{13} and R^{14} independently of each other are selected from hydroxy, perhalomethyl, C_{1-6}-alkoxy or amino optionally substituted with one or more C_{1-6}-alkyl, perhalomethyl or aryl optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano];

------ represents a single bond or a double bond;

Ar is arylene[,] or heteroarylene[, or a divalent heterocyclic group each of which is optionally substituted with one or more halogen, C_{1-6}-alkyl, amino, hydroxy, C_{1-6}-alkoxy or aryl];

R^5 is hydrogen[, hydroxy, halogen, C_{1-12}-alkoxy, C_{1-12}-alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl or arylalkyl optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano or R^5 forms a bond together with R^6];

R^6 is hydrogen[, hydroxy, halogen, C_{1-12}-alkoxy, C_{1-12}-alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl, acyl or arylalkyl optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano or R^6 forms a bond together with R^5];

M is OR^7, where R^7 is hydrogen, C_{1-12}-alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl, aryl, arylalkyl, C_{1-12}-alkoxyC_{1-12}-alkyl, C_{1-12}-alkoxycarbonyl, aryloxycarbonyl, C_{1-12}-alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroarylalkyl groups optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano or M is $COYR^8$;

R^8 is hydrogen, C_{1-12}alkyl, C_{4-12}-alkenynyl, C_{2-12}-alkenyl, C_{2-12}-alkynyl[, aryl, arylalkyl, heterocyclyl, heteroaryl or heteroarylalkyl groups optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano];

Y is oxygen[, sulphur or NR^{10}, where R^{10} is hydrogen, C_{1-12}-alkyl, aryl, hydroxyC_{1-12}-alkyl or arylalkyl groups or when Y is NR^{10}, R^8 and R^{10} may form a 5 or 6 membered nitrogen containing ring, optionally substituted with one or more C_{1-6}-alkyl];

k is an integer [ranging] from 1 to 2, n [is an integer ranging from 0 to 3] and m [is an integer ranging from 0 to] are 1;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, or any tautomeric forms.

2. (Amended) [A] The compound of claim 1, wherein A^1 and A^2 are independently of each other a 5-6 membered cyclic ring [or a 9-10 membered bicyclic ring,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, C_{1-6}-alkyl, (C_{3-6}-cycloalkyl)C_{1-6}-alkyl, C_{4-6}-alkenynyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{1-6}-alkoxy, aryl, aryloxy, arylalkyl, arylalkoxy, heterocyclyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, acyl, hydroxyC_{1-6}-alkyl, C_{1-6}-alkyl-amino, C_{1-6}-dialkylamino, arylamino, arylalkylamino, aminoC_{1-6}-alkyl, C_{1-6}-alkoxycarbonyl, alkylaminocarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, C_{1-6}-alkoxyC_{1-6}-alkyl, aryloxyC_{1-6}-alkyl, or arylalkoxyC_{1-6}-alkyl.

3. (Amended) [A] The compound of claim 1, wherein A^1 and A^2 are independently of each other a 5-6 membered cyclic ring [or a 9-10 membered bicyclic ring,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, C_{1-6}-alkyl, (C_{3-6}-cycloalkyl)C_{1-6}-alkyl, C_{4-6}-alkenynyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, C_{1-6}-alkoxy, aryl, aryloxy, arylalkyl, arylalkoxy, heterocyclyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, acyl, hydroxyC_{1-6}-alkyl, C_{1-6}-alkyl-amino, C_{1-6}-dialkylamino, arylamino, arylalkylamino, aminoC_{1-6}-alkyl, C_{1-6}-alkoxyC_{1-6}-alkyl, aryloxyC_{1-6}-alkyl, or arylalkoxyC_{1-6}-alkyl.

4. (Amended) [A] The compound of claim 1, wherein A^1 and A^2 are independently of each other a 5-6 membered cyclic ring [or a 9-10 membered bicyclic ring,] optionally substituted with one or more halogen, C_{1-6}-alkyl, C_{1-6}-alkoxy or aryl.

5. (Amended) [A] The compound of claim 1, wherein A^1 and A^2 are independently of each other a 5-6 membered cyclic ring optionally substituted with one or more halogen, C_{1-6}-alkyl, C_{1-6}-alkoxy, or aryl.

15. (Amended) [A] The compound of claim 1, wherein Ar is arylene, or heteroarylene.

16. (Amended) [A] The compound of claim 1, wherein Ar is arylene.

25. (Amended) [A] The compound of claim 1, wherein M is OR^7, where R^7 is hydrogen, C_{1-6}-alkyl, C_{4-6}-alkenynyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, aryl, arylalkyl, C_{1-6}-alkoxyC_{1-6}-alkyl, C_{1-6}-alkoxycarbonyl, aryloxycarbonyl, C_{1-6}-alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroarylalkyl groups optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano.

26. (Amended) [A] The compound of claim 1, wherein M is OR^7, where R^7 is hydrogen, C_{1-6}-alkyl, C_{4-6}-alkenynyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, aryl, arylalkyl, C_{1-6}-alkoxyC_{1-6}-alkyl, heterocyclyl, heteroaryl or heteroarylalkyl groups optionally substituted with one or more halogen or perhalomethyl.

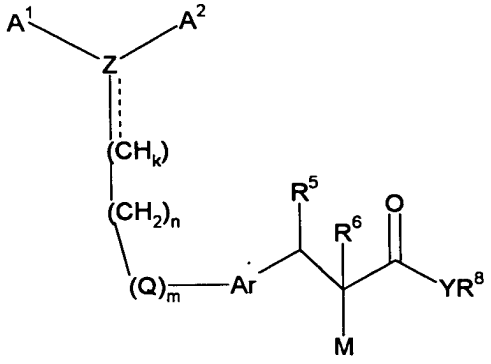
27. (Amended) [A] The compound of claim 1, wherein M is OR^7, where R^7 is C_{1-6}-alkyl or M is $COYR^8$ where R^8 is defined as in claim 1.

28. (Amended) [A] The compound of claim 1, wherein M is OR^7, where R^7 is ethyl or M is $COYR^8$ where R^8 is defined as in claim 1.

31. (Amended) [A] The compound of claim 1, wherein R^8 is hydrogen or C_{1-6}alkyl.

32. (Amended) [A] The compound of claim 1, wherein R^8 is hydrogen or ethyl.

38. (Amended) A compound of [claim 1, which is] formula (I)



selected from the group consisting of:

2-Ethoxy-3-{4-[3-phenyl-3-(4-methylphenyl)-allyloxy]-phenyl}-propionic acid ethyl ester,

2-Ethoxy-3-{4-[3-phenyl-3-(4-methylphenyl)-allyloxy]-phenyl}-propionic acid,

3-{4-[3-(2-Chloro-phenyl)-3-phenyl-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

3-{4-[3-(2-Chloro-phenyl)-3-phenyl-allyloxy]-phenyl}-2-ethoxy-propionic acid,

3-{4-[3,3-Bis-(4-methoxy-phenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

3-{4-[3,3-Bis-(4-methoxy-phenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid,

3-{4-[3-Phenyl-3-(biphenyl-4-yl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

3-{4-[3-Phenyl-3-(biphenyl-4-yl)-allyloxy]-phenyl}-2-ethoxy-propionic acid,

2-Ethoxy-3-{4-[3-phenyl-3-(thiophen-2-yl)-allyloxy]-phenyl}-propionic acid ethyl ester,

2-Ethoxy-3-{4-[3-phenyl-3-(thiophen-2-yl)-allyloxy]-phenyl}-propionic acid,

2-Ethoxy-3-{4-[3-phenyl-3-(pyridin-2-yl)-allyloxy]-phenyl}-propionic acid ethyl ester,

2-Ethoxy-3-{4-[3-phenyl-3-(pyridin-2-yl)-allyloxy]-phenyl}-propionic acid,

3-[4-(3, 3-Diphenyl-propoxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

3-[4-(3,3-Diphenyl-propoxy)-phenyl]-2-ethoxy-propionic acid,

2-Ethoxy-3-{4-[3-phenyl-3-(4-methylphenyl)-propoxy]-phenyl}-propionic acid ethyl ester,

2-Ethoxy-3-{4-[3-phenyl-3-(4-methylphenyl)-propoxy]-phenyl}-propionic acid,

3-{4-[3-Phenyl-3-(biphenyl-4-yl)-propoxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

3-{4-[3-Phenyl-3-(biphenyl-4-yl)-propoxy]-phenyl}-2-ethoxy-propionic acid,

2-{4-[3,3-Bis-(4-methoxy-phenyl)-allyloxy]-benzyl}-malonic acid dimethyl ester,

(*E*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-furan-2-yl-phenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid ethyl ester,

(*E*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-furan-2-yl-phenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid,

(*E*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-phenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

(*E*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-phenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid,

(*E, Z*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-phenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

(*E, Z*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-phenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid,

3-{4-[3,3-Bis-(3-methyl-thiophen-2-yl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

3-{4-[3,3-Bis-(4-bromo-phenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

3-{4-[3,3-Bis-(4-bromo-phenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid,

2-Ethoxy-3-[4-(3-phenyl-3-pyridin-4-yl-allyloxy)-phenyl]-propionic acid ethyl ester,

2-Ethoxy-3-[4-(3-phenyl-3-pyridin-4-yl-allyloxy)-phenyl]-propionic acid,

(*E, Z*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-methoxyphenyl)-3-thiophen-2-yl-allyloxy]-phenyl}-propionic acid ethyl ester,

(*E, Z*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-methoxyphenyl)-3-thiophen-2-yl-allyloxy]-phenyl}-propionic acid,

(*E, Z*)-(2*S*)-2-Ethoxy-3-[4-(3-phenyl-3-p-tolyl-allyloxy)-phenyl]-propionic acid ethyl ester,

(*E, Z*)-(2*S*)-2-Ethoxy-3-[4-(3-phenyl-3-p-tolyl-allyloxy)-phenyl]-propionic acid,

(2*S*)-3-[4-(3,3-Diphenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

(2*S*)-3-[4-(3,3-Diphenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid,

(*Z*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-fluorophenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid ethyl ester,

(*Z*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-fluorophenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid,

(*E*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-fluorophenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid ethyl ester,

(*E*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-fluorophenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid,

(2*S*)-3-{4-[3,3-Bis-(4-methoxyphenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

(2*S*)-3-{4-[3,3-Bis-(4-methoxyphenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid,

(2*S*)-3-[4-(3,3-Di-p-tolyl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

(2*S*)-3-[4-(3,3-Di-p-tolyl-allyloxy)-phenyl]-2-ethoxy-propionic acid,

(*Z*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-phenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid,

(*Z*)-(2*S*)-3-{4-[3-(4-Bromophenyl)-3-phenyl-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

(*Z*)-(2*S*)-3-{4-[3-(4-Bromophenyl)-3-phenyl-allyloxy]-phenyl}-2-ethoxy-propionic acid,

(2*S*)-3-[4-(3,3-Bis-biphenyl-4-yl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

(2*S*)-3-[4-(3,3-Bis-biphenyl-4-yl-allyloxy)-phenyl]-2-ethoxy-propionic acid,

(2*S*)-3-{4-[3,3-Bis-(4-bromophenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

(2*S*)-3-{4-[3,3-Bis-(4-bromophenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid,

(*Z*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-furan-2-yl-phenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid ethyl ester,

(*Z*)-(2*S*)-2-Ethoxy-3-{4-[3-(4-furan-2-yl-phenyl)-3-phenyl-allyloxy]-phenyl}-propionic acid,

(*E*)-(2*S*)-3-{4-[3-(4-Bromophenyl)-3-phenyl-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

(*E*)-(2*S*)-3-{4-[3-(4-Bromophenyl)-3-phenyl-allyloxy]-phenyl}-2-ethoxy-propionic acid,

(2*S*)-3-{4-[3,3-Bis-(4-furan-2-yl-phenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid ethyl ester,

(2*S*)-3-{4-[3,3-Bis-(4-furan-2-yl-phenyl)-allyloxy]-phenyl}-2-ethoxy-propionic acid,

(*E*, *Z*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-p-tolyl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester,

(*E*, *Z*)-(2*S*)-3-[4-(3-Biphenyl-4-yl-3-p-tolyl-allyloxy)-phenyl]-2-ethoxy-propionic acid, or

(*E*, *Z*)-(2*R*)- 3-[4-(3-Biphenyl-4-yl-3-phenyl-allyloxy)-phenyl]-2-ethoxy-propionic acid ethyl ester;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, or any tautomeric forms.

39. (Amended) A pharmaceutical composition comprising, as an active ingredient, an effective amount of [a] the compound of claim 1, together with a pharmaceutically acceptable carrier or diluent.

40. The pharmaceutical composition of claim 39 in unit dosage form, comprising from about 0.05 to about 100 mg of the compound.

41. The pharmaceutical composition of claim 40 in unit dosage form, comprising from about 0.1 to about 50 mg of the compound.

42. The pharmaceutical composition of claim 39 which is administered by the oral, nasal, transdermal, pulmonary, or parenteral route.